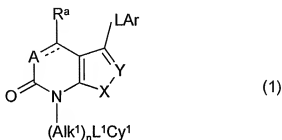


This listing of claims will replace all prior versions, and listings, of claims in the application.

I. Listing of Claims:

1. (currently amended) A compound of formula (1):



wherein

the dashed line joining A and C(R^a) is present and represents a bond and A is a -N= atom or a -C(R^b)= group, or the dashed line is absent and A is a -N(R^b)- or -C(R^b)(R^c)- group;

R^a, and R^b are both hydrogen and R^c ~~are each independently~~ is a hydrogen atom or an optionally substituted C₁₋₆ alkyl, -CN, -CO₂H, -CO₂R¹, -CONH₂, -CONHR¹ or -CONR¹R² group;

R¹ and R² are each, independently, an optionally substituted alkyl group;

X is an -O-, -S- or substituted nitrogen atom or a -S(O)-, -S(O)₂- or -NH- group;

Y is a nitrogen or substituted carbon atom, or a -CH= group, or -C(R¹⁰)= in which R¹⁰ is -CN, -CONH₂, -CONHet¹, -CON(R¹²)Het², -CON(R¹²)Alk⁵Het² or -CO₂Alk⁶ wherein -NHet¹ is pyrrolidinyl, imidazolidinyl, pyrazolidinyl, piperazinyl, morpholinyl,

thiomorpholinyl, piperidinyl or thiazolidinyl, R^{12} is a hydrogen atom or a straight or branched C_{1-6} alkyl group, -Het² is cyclopentyl, cyclohexyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, piperazinyl, morpholinyl, thiomorpholinyl, piperidinyl or thiazolidinyl, Alk⁵ is a straight or branched C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene chain, optionally interrupted by one, two or three -O- or -S- atoms or -S(O)-, -S(O)₂- or -N(R¹²)- groups, and Alk⁶ is C_{1-4} alkyl;

n is zero or the integer 1;

Alk¹ is an optionally-substituted aliphatic or heteroaliphatic chain optionally substituted with one, two, three or more substituents where each substituent may be the same or different and is selected from halogen atoms, -OH, -CO₂H, -CO₂R⁴, -CO₂CH₃, -CON(CH₃)₂, -CONHR⁴, -CON(R⁴)₂, -COR⁴, C_{1-6} alkoxy, halo(C_{1-6})alkoxy, -SH, -S(O)R⁴, -S(O)₂R⁴, C_{1-6} alkylthio, NHR⁴, and -N(R⁴)₂, where R⁴ is an optionally substituted straight or branched C_{1-6} alkyl group, and such that where two R⁴ groups are present they may be the same or different and, if attached to an N atom may be joined, together with the N atom to which they are attached, to form a heterocyclic ring, which heterocyclic ring may be optionally interrupted by a further heteroatom or heteroatom-containing group selected from -O-, -S-, -N(R⁴)-, -C(O)- or -C(S)-;

L¹ is a covalent bond or a linker atom or group, said linker atom or group being selected from -O-, -S-, -C(O)-, -C(O)O-, -OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R³)-, -N(R³)O-, -N(R³)NH-, -CON(R³)-, -OC(O)N(R³)-, -CSN(R³)-, -N(R³)CO-, -(R³)C(O)O-, -N(R³)CS-, -S(O)₂N(R³)-, -N(R³)S(O)₂-, -N(R³)CON(R³)-,

-N(R³)CSN(R³)- and -N(R³)SO₂N(R³)-, where R³ is a hydrogen atom or a straight or branched alkyl group, and such that where L¹ contains two R³ groups these may be the same or different;

Cy¹ is a hydrogen atom or an optionally substituted cycloaliphatic, polycycloaliphatic, heterocycloaliphatic, polyheterocycloaliphatic, aromatic or heteroaromatic group, said optional substituent being selected from halogen, C₁₋₆ alkyl, halo(C₁₋₆ alkyl), C₁₋₆ alkoxy, halo(C₁₋₆ alkoxy), cyano, -CO₂CH₃, -CO₂C(CH₃)₃, nitro, amino, -NHCH₃, -N(CH₃)₂, -COCH₃ and -NHCOCH₃;

L is an atom or chain -(CH₂)_pHet(CH₂)_q;

p and q, which may be the same or different, are each zero or the integer 1;

Het is an -O- or -S- atom or a -C(R^{3a})(R^{3b})-, -C(O)-, -C(O)O-, -OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R^{3c})O-, -N(R^{3c})NH-, -N(R^{3c})C(R^{3a})(R^{3b})-, -CON(R^{3c})-, -OC(O)N(R^{3c})-, -CSN(R^{3c})-, -N(R^{3c})CO-, -N(R^{3c})C(O)O-, -N(R^{3c})CS-, -S(O)₂N(R^{3c})-, -N(R^{3c})S(O)₂-, -N(R^{3c})CON(R^{3d})-, -N(R^{3c})CSN(R^{3d})- or -N(R^{3c})S(O)₂N(R^{3d})- group and, when one or both of p and q is the integer 1, Het is additionally a -N(R^{3c})- group;

R^{3a} and R^{3b} are each independently a hydrogen atom, -OH, or an optionally substituted C₁₋₆ alkyl group;

R^{3c} and R^{3d} are each independently a hydrogen atom or a straight or branched alkyl group;

Ar is an optionally substituted aromatic or heteroaromatic group;
or a pharmaceutically acceptable salt, ~~solvate, hydrate, or N-oxide thereof.~~

2. (previously presented) A compound as claimed in claim 1 wherein the dashed line joining A and C(R^a) is present and represents a bond and A is a -C(R^b)= group.
3. (cancelled)
4. (previously presented) A compound as claimed in claim 1 wherein X is -S-.
5. (previously presented) A compound as claimed in claim 1 wherein Y is -C(R¹⁰)= in which R¹⁰ is -CN, -CONH₂ or -CO₂Alk⁶ and Alk⁶ is C₁₋₄ alkyl.
6. (previously presented) A compound as claimed in claim 1 wherein Cy¹ is phenyl or cyclopropyl.
7. (previously presented) A compound as claimed in claim 1 wherein Ar represents phenyl, halophenyl, dihalophenyl, (C₁₋₆ alkyl)phenyl, pyridinyl or (C₁₋₆ alkyl)pyridinyl.
8. (previously presented) A compound as claimed in claim 1 selected from
- Ethyl 3-(benzylamino)-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 3-(*N*-benzyl-*N*-methylamino)-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 6-oxo-7-phenyl-3-[(1-phenylethyl)amino]-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 3-[(2,6-difluorobenzyl)amino]-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 3-benzyl-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 6-oxo-3-phenoxy-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 6-oxo-7-phenyl-3-(phenylthio)-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 6-oxo-7-phenyl-3-[(pyridin-2-ylmethyl)amino]-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

3-(Benzylamino)-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carbonitrile;

6-Oxo-7-phenyl-3-(phenylthio)-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxamide;

Ethyl 3-(benzoylamino)-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 6-oxo-7-phenyl-3-[(phenylsulphonyl)amino]-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 3-[(anilinoacetyl)amino]-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 6-oxo-7-phenyl-3-(2-phenylethyl)-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 3-[hydroxy(phenyl)methyl]-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 3-[hydroxy(6-methylpyridin-2-yl)methyl]-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 3-[hydroxy(3-methylphenyl)methyl]-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

3-[Hydroxy(phenyl)methyl]-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carbonitrile;

3-[Hydroxy(3-methylphenyl)methyl]-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carbonitrile;

Ethyl 7-(cyclopropylmethyl)-3-[hydroxy(phenyl)methyl]-6-oxo-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 3-(anilinosulfonyl)-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 3-[(3-methylphenyl)thio]-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate;

Ethyl 3-[2-(4-methylphenyl)hydrazino]-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate; and

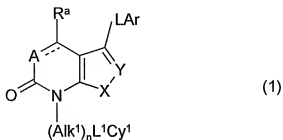
Ethyl 3-[(3-chlorophenyl)(hydroxy)methyl]-6-oxo-7-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-2-carboxylate.

9. (currently amended) A pharmaceutical composition comprising a compound of claim 1, or a pharmaceutically acceptable salt, ~~solvate, hydrate or N-oxide~~ thereof, in association with a pharmaceutically acceptable carrier.

10-11. (canceled)

12. (currently amended and withdrawn) A method for inhibiting p38 kinase in a patient suffering from a disease or disorder in which p38 kinase plays a role, comprising

administering to the patient a pharmaceutically effective amount of a compound of formula 1:



wherein

the dashed line joining A and C(R^a) is present and represents a bond and A is a -N= atom or a -C(R^b)= group, or the dashed line is absent and A is a -N(R^b)- or -C(R^b)(R^c)- group;

R^a, and R^b are both hydrogen and R^c are each independently is a hydrogen atom or an optionally substituted C₁₋₆ alkyl, -CN, -CO₂H, -CO₂R¹, -CONH₂, -CONHR¹ or -CONR¹R² group;

R¹ and R² are each, independently, an optionally substituted alkyl group;

X is an -O-, -S- or substituted nitrogen atom or a -S(O)-, -S(O)₂- or -NH- group;

Y is a nitrogen or substituted carbon atom, or a -CH= group, or -C(R¹⁰)= in which R¹⁰ is -CN-, -CONH₂, -CONHet¹, -CON(R¹²)Het², -CON(R¹²)Alk⁵Het² or -CO₂Alk⁶ wherein -NHet¹ is pyrrolidinyl, imidazolidinyl, pyrazolidinyl, piperazinyl, morpholinyl, thiomorpholinyl, piperidinyl or thiazolidinyl, R¹² is a hydrogen atom or a straight or

branched C₁₋₆ alkyl group, -Het² is cyclopentyl, cyclohexyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, piperazinyl, morpholinyl, thiomorpholinyl, piperidinyl or thiazolidinyl, Alk⁵ is a straight or branched C₁₋₆ alkylene, C₂₋₆ alkenylene or C₂₋₆ alkynylene chain, optionally interrupted by one, two or three -O- or -S- atoms or -S(O)-, -S(O)₂- or -N(R¹³)- groups, and Alk⁶ is C₁₋₄ alkyl;

n is zero or the integer 1;

Alk¹ is an optionally-substituted aliphatic or heteroaliphatic chain optionally substituted with one, two, three or more substituents where each substituent may be the same or different and is selected from halogen atoms, -OH, -CO₂H, -CO₂R⁴, -CO₂CH₃, -CON(CH₃)₃, -CONHR⁴, -CON(R⁴)₂, -COR⁴, C₁₋₆ alkoxy, halo(C₁₋₆)alkoxy, -SH, -S(O)R⁴, -S(O)₂R⁴, C₁₋₆ alkylthio, NHR⁴, and -N(R⁴)₂, where R⁴ is an optionally substituted straight or branched C₁₋₆ alkyl group, and such that where two R⁴ groups are present they may be the same or different and, if attached to an N atom may be joined, together with the N atom to which they are attached, to form a heterocyclic ring, which heterocyclic ring may be optionally interrupted by a further heteroatom or heteroatom-containing group selected from -O-, -S-, -N(R⁴)-, -C(O)- or -C(S)-;

L¹ is a covalent bond or a linker atom or group, said linker atom or group being selected from -O-, -S-, -C(O)-, -C(O)O-, -OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R³)-, -N(R³)O-, -N(R³)NH-, -CON(R³)-, -OC(O)N(R³)-, -CSN(R³)-, -N(R³)CO-, -(R³)C(O)O-, -N(R³)CS-, -S(O)₂N(R³)-, -N(R³)S(O)₂-, -N(R³)CON(R³)-,

-N(R³)CSN(R³)- and -N(R³)SO₂N(R³)-, where R³ is a hydrogen atom or a straight or branched alkyl group, and such that where L¹ contains two R³ groups these may be the same or different;

Cy¹ is a hydrogen atom or an optionally substituted cycloaliphatic, polycycloaliphatic, heterocycloaliphatic, polyheterocycloaliphatic, aromatic or heteroaromatic group, said optional substituent being selected from halogen, C₁₋₆ alkyl, halo(C₁₋₆ alkyl), C₁₋₆ alkoxy, halo(C₁₋₆ alkoxy), cyano, -CO₂CH₃, -CO₂C(CH₃)₃, nitro, amino, -NHCH₃, -N(CH₃)₂, -COCH₃ and -NHCOCH₃;

L is an atom or chain -(CH₂)_pHet(CH₂)_q;

p and q, which may be the same or different, are each zero or the integer 1;

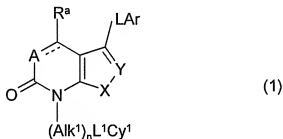
Het is an -O- or -S- atom or a -C(R^{3a})(R^{3b})-, -C(O)-, -C(O)O-, -OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R^{3c})O-, -N(R^{3c})NH-, -N(R^{3c})C(R^{3a})(R^{3b})-, -CON(R^{3c})-, -OC(O)N(R^{3c})-, -CSN(R^{3c})-, -N(R^{3c})CO-, -N(R^{3c})C(O)O-, -N(R^{3c})CS-, -S(O)₂N(R^{3c})-, -N(R^{3c})S(O)₂-, -N(R^{3c})CON(R^{3d})-, -N(R^{3c})CSN(R^{3d})- or -N(R^{3c})S(O)₂N(R^{3d})- group and, when one or both of p and q is the integer 1, Het is additionally a -N(R^{3c})- group;

R^{3a} and R^{3b} are each independently a hydrogen atom, -OH, or an optionally substituted C₁₋₆ alkyl group;

R^{3c} and R^{3d} are each independently a hydrogen atom or a straight or branched alkyl group;

Ar is an optionally substituted aromatic or heteroaromatic group;
or a pharmaceutically acceptable prodrug, or salt, solvate, hydrate, or N-oxide thereof.

13. (currently amended and withdrawn) A method for the treatment of autoimmune diseases, inflammatory diseases, destructive bone disorders, proliferative disorders, neurodegenerative disorders, viral diseases, allergies, infectious diseases, heart attacks, angiogenic disorders, reperfusion/ischemia in stroke, vascular hyperplasia, organ hypoxia, cardiac hypertrophy, thrombin-induced platelet aggregation, and conditions associated with prostaglandin endoperoxidase synthetase-2, comprising administering to a patient suffering from such a disease or disorder a pharmaceutically effective amount of a compound of formula 1:



wherein

the dashed line joining A and C(R^a) is present and represents a bond and A is a -N= atom or a -C(R^b)= group, or the dashed line is absent and A is a -N(R^b)- or -C(R^b)(R^c)- group;

R^a, and R^b are both hydrogen and R^c are each independently is a hydrogen atom or an optionally substituted C₁₋₆ alkyl, -CN, -CO₂H, -CO₂R¹, -CONH₂, -CONHR¹ or -CONR¹R² group;

R¹ and R² are each, independently, an optionally substituted alkyl group;

X is an -O-, -S- or substituted nitrogen atom or a -S(O)-, -S(O)₂- or -NH- group;

Y is a nitrogen or substituted carbon atom, or a -CH= group, or $\text{-C(R}^{10})\text{=}$ in which R^{10} is -CN- , -CONH_2 , -CONHet^1 , $\text{-CON(R}^{12})\text{Het}^2$, $\text{-CON(R}^{12})\text{Alk}^5\text{Het}^2$ or $\text{-CO}_2\text{Alk}^6$ wherein -NHet^1 is pyrrolidinyl, imidazolidinyl, pyrazolidinyl, piperazinyl, morpholinyl, thiomorpholinyl, piperidinyl or thiazolidinyl, R^{12} is a hydrogen atom or a straight or branched C_{1-6} alkyl group, -Het^2 is cyclopentyl, cyclohexyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, piperazinyl, morpholinyl, thiomorpholinyl, piperidinyl or thiazolidinyl, Alk^5 is a straight or branched C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene chain, optionally interrupted by one, two or three -O- or -S- atoms or -S(O)- , $\text{-S(O)}_2\text{-}$ or $\text{-N(R}^{12})\text{-}$ groups, and Alk^6 is C_{1-4} alkyl;

n is zero or the integer 1;

Alk^1 is an optionally substituted aliphatic or heteroaliphatic chain optionally substituted with one, two, three or more substituents where each substituent may be the same or different and is selected from halogen atoms, -OH- , $\text{-CO}_2\text{H-}$, $\text{-CO}_2\text{R}^4$, $\text{-CO}_2\text{CH}_3$, $\text{-CON(CH}_3)_3$, -CONHR^4 , $\text{-CON(R}^4)_2$, -COR^4 , C_{1-6} alkoxy, halo(C_{1-6})alkoxy, -SH- , -S(O)R^4 , $\text{-S(O)}_2\text{R}^4$, C_{1-6} alkylthio, NHR^4 , and $\text{-N(R}^4)_2$, where R^4 is an optionally substituted straight or branched C_{1-6} alkyl group, and such that where two R^4 groups are present they may be the same or different and, if attached to an N atom may be joined, together with the N atom to which they are attached, to form a heterocyclic ring, which heterocyclic ring may be optionally interrupted by a further heteroatom or heteroatom-containing group selected from -O- , -S- , $\text{-N(R}^4)\text{-}$, -C(O)- or -C(S)- ;

L^1 is a covalent bond or a linker atom or group, said linker atom or group being selected from -O- , -S- , -C(O)- , -C(O)O- , -OC(O)- , -C(S)- , -S(O)- , $\text{-S(O)}_2\text{-}$, $\text{-N(R}^3)\text{-}$, $\text{-N(R}^3)\text{O-}$, $\text{-N(R}^3)\text{NH-}$, $\text{-CON(R}^3)\text{-}$, $\text{-OC(O)N(R}^3)\text{-}$, $\text{-CSN(R}^3)\text{-}$, $\text{-N(R}^3)\text{CO-}$,

$-(R^3)C(O)O-$, $-N(R^3)CS-$, $-S(O)_2N(R^3)-$, $-N(R^3)S(O)_2-$, $-N(R^3)CON(R^3)-$,

$-N(R^3)CSN(R^3)-$ and $-N(R^3)SO_2N(R^3)-$, where R^3 is a hydrogen atom or a straight or branched alkyl group, and such that where L^1 contains two R^3 groups these may be the same or different;

Cy^1 is a hydrogen atom or an optionally substituted cycloaliphatic, polycycloaliphatic, heterocycloaliphatic, polyheterocycloaliphatic, aromatic or heteroaromatic group, said optional substituent being selected from halogen, C_{1-6} alkyl, halo(C_{1-6} alkyl), C_{1-6} alkoxy, halo(C_{1-6} alkoxy), cyano, $-CO_2CH_3$, $-CO_2C(CH_3)_3$, nitro, amino, $-NHCH_3$, $-N(CH_3)_2$, $-COCH_3$ and $-NHCOCH_3$;

L is an atom or chain $-(CH_2)_pHet(CH_2)_q-$;

p and q , which may be the same or different, are each zero or the integer 1;

Het is an $-O-$ or $-S-$ atom or a $-C(R^{3a})(R^{3b})-$, $-C(O)-$, $-C(O)O-$, $-OC(O)-$, $-C(S)-$, $-S(O)-$, $-S(O)_2-$, $-N(R^{3c})O-$, $-N(R^{3c})NH-$, $-N(R^{3c})C(R^{3a})(R^{3b})-$, $-CON(R^{3c})-$, $-OC(O)N(R^{3c})-$, $-CSN(R^{3c})-$, $-N(R^{3c})CO-$, $-N(R^{3c})C(O)O-$, $-N(R^{3c})CS-$, $-S(O)_2N(R^{3c})-$, $-N(R^{3c})S(O)_2-$, $-N(R^{3c})CON(R^{3d})-$, $-N(R^{3c})CSN(R^{3d})-$ or $-N(R^{3c})S(O)_2N(R^{3d})-$ group and, when one or both of p and q is the integer 1, Het is additionally a $-N(R^{3e})-$ group;

R^{3a} and R^{3b} are each independently a hydrogen atom, $-OH$, or an optionally substituted C_{1-6} alkyl group;

R^{3c} and R^{3d} are each independently a hydrogen atom or a straight or branched alkyl group;

Ar is an optionally substituted aromatic or heteroaromatic group;

or a pharmaceutically acceptable prodrug, or salt, ~~solvate, hydrate, or N-oxide~~ thereof.

14. (withdrawn) The method of claim 13 wherein the autoimmune diseases are selected from the group consisting of rheumatoid arthritis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, multiple sclerosis, diabetes, glomerulonephritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Grave's disease, hemolytic anemia, autoimmune gastritis, autoimmune neutropenia, thrombocytopenia, chronic active hepatitis, myasthenia gravis, atopic dermatitis, graft vs host disease, and psoriasis.

15. (withdrawn) The method of claim 13 wherein the inflammatory diseases are selected from the group consisting of asthma, allergies, respiratory distress syndrome, and acute or chronic pancreatitis.

16. (withdrawn) The method of claim 13 wherein the destructive bone disorders are selected from the group consisting of osteoporosis, osteoarthritis, and multiple myeloma-related bone disorder.

17. (withdrawn) The method of claim 13 wherein the proliferative disorders are selected from the group consisting of chronic myelogenous leukemia, Kaposi's sarcoma, metastatic melanoma and multiple myeloma.

18. (withdrawn) The method of claim 13 wherein the neurodegenerative disorders are selected from the group consisting of Parkinson's disease, Alzheimer's disease, cerebral ischemias and neurodegenerative disease caused by traumatic injury.
19. (withdrawn) The method of claim 13 wherein the viral diseases are selected from the group consisting of hepatitis A infection, hepatitis B infection, hepatitis C infection, HIV infection, and CMV retinitis.
20. (withdrawn) The method of claim 13 wherein the infections diseases are selected from the group consisting of septic shock, sepsis, and Shigellosis.
21. (withdrawn) The method of claim 13 wherein the conditions associated with prostaglandin endoperoxidase synthetase-2 are selected from the group consisting of edema, analgesia, fever, neuromuscular pain, headache, dental pain, arthritis pain, and pain caused by cancer.